



Efficacia della semaglutide nel paziente obeso a rischio CV

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Regione
Lombardia



UNIVERSITÀ
DI PAVIA



Why Cardiologists Should Pay Attention to Obesity

1 Obesity is an increasing disease

2 Obesity partners with CVD

3 Obesity is a complex syndrome

4 Obesity can be treated

Obesity
and Cardiovascular Disease Risk



Obesity is a Chronic Progressive and Relapsing Disease

Overweight and obesity

are major risk factors for several chronic diseases, including diabetes, cardiovascular diseases and cancer

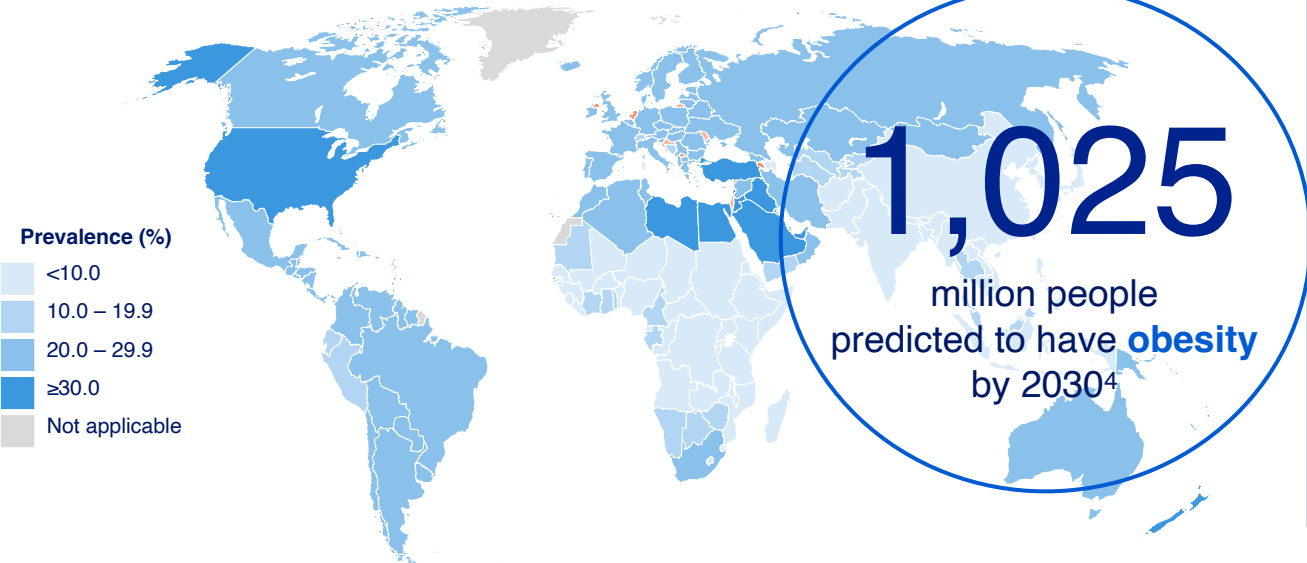
**BMI**

=

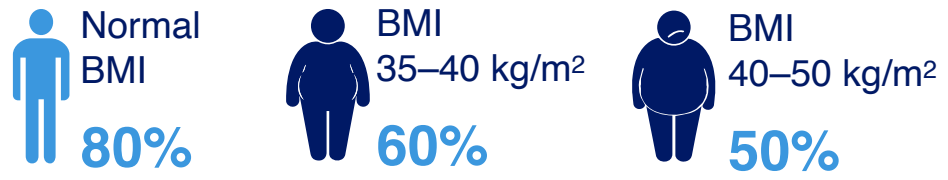
$$\frac{\text{weight (kg)}}{\text{height}^2 \text{ (m}^2\text{)}}$$

Body mass index provides the most convenient population-level measure of overweight and obesity

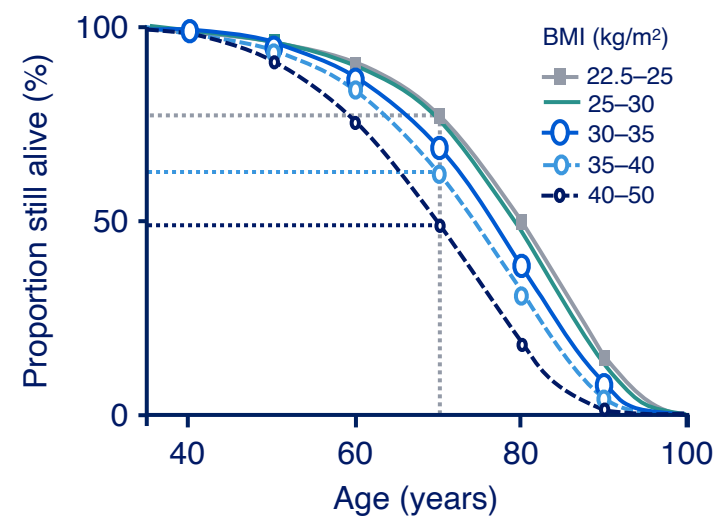
Obesity rates are increasing globally



Life expectancy decreases as BMI increases



↓ chance of reaching age 70

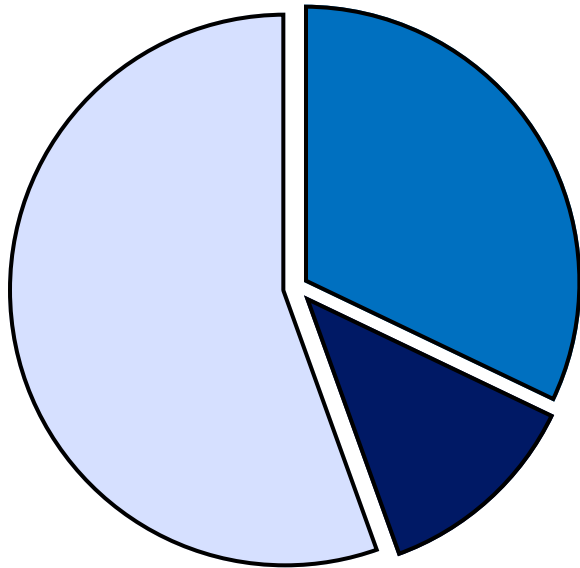


WHO. Global Health Observatory (GHO) data. Prevalence of obesity among adults. Available from https://www.who.int/gho/ncd/risk_factors/overweight_obesity/obesity_adults/en/ . Accessed May 2020; WHO, Obesity & Overweight. Available from <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>. Accessed May 2020. Prospective Studies Collaboration. Lancet 2009;373:1083–96.

15-Year Incidence of Overweight/Obesity in Natiowide Italian Registries on ACS



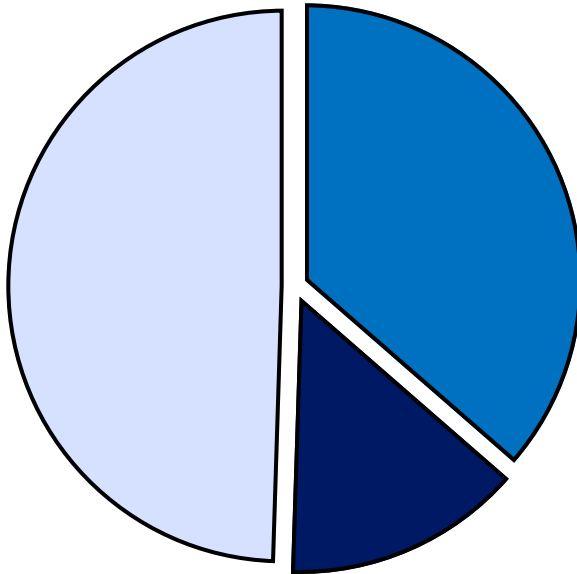
2009



● BMI 25-30 ● BMI >30 ○ BMI <25



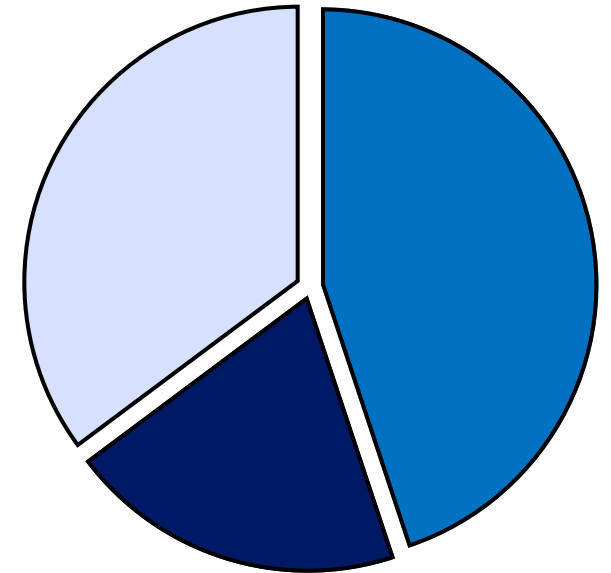
2014



● BMI 25-30 ● BMI >30 ○ BMI <25



2024



● BMI 25-30 ● BMI >30 ○ BMI <25

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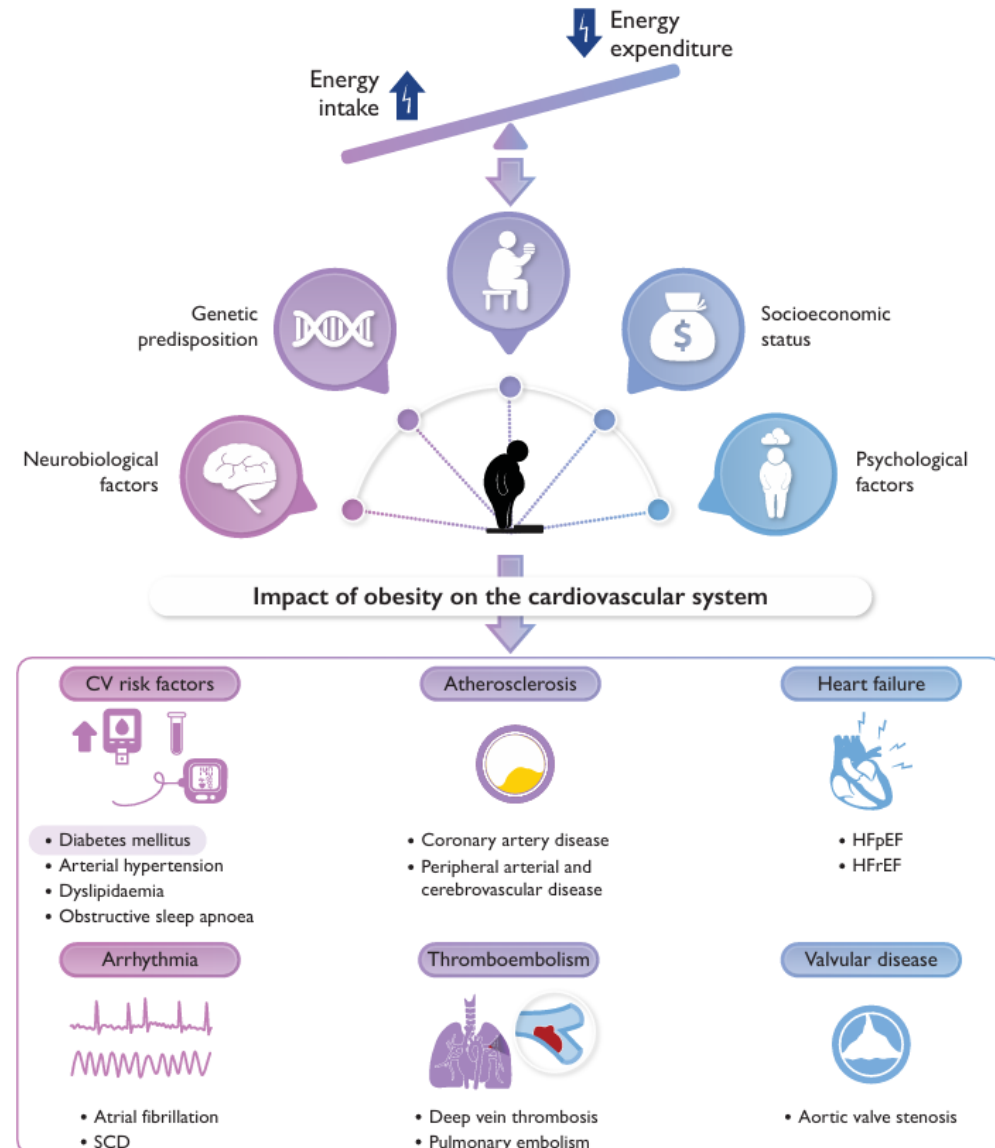
3 Obesity is a complex syndrome

4 Obesity can be treated

Obesity
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Main Causal Factors and CV Consequences of Obesity



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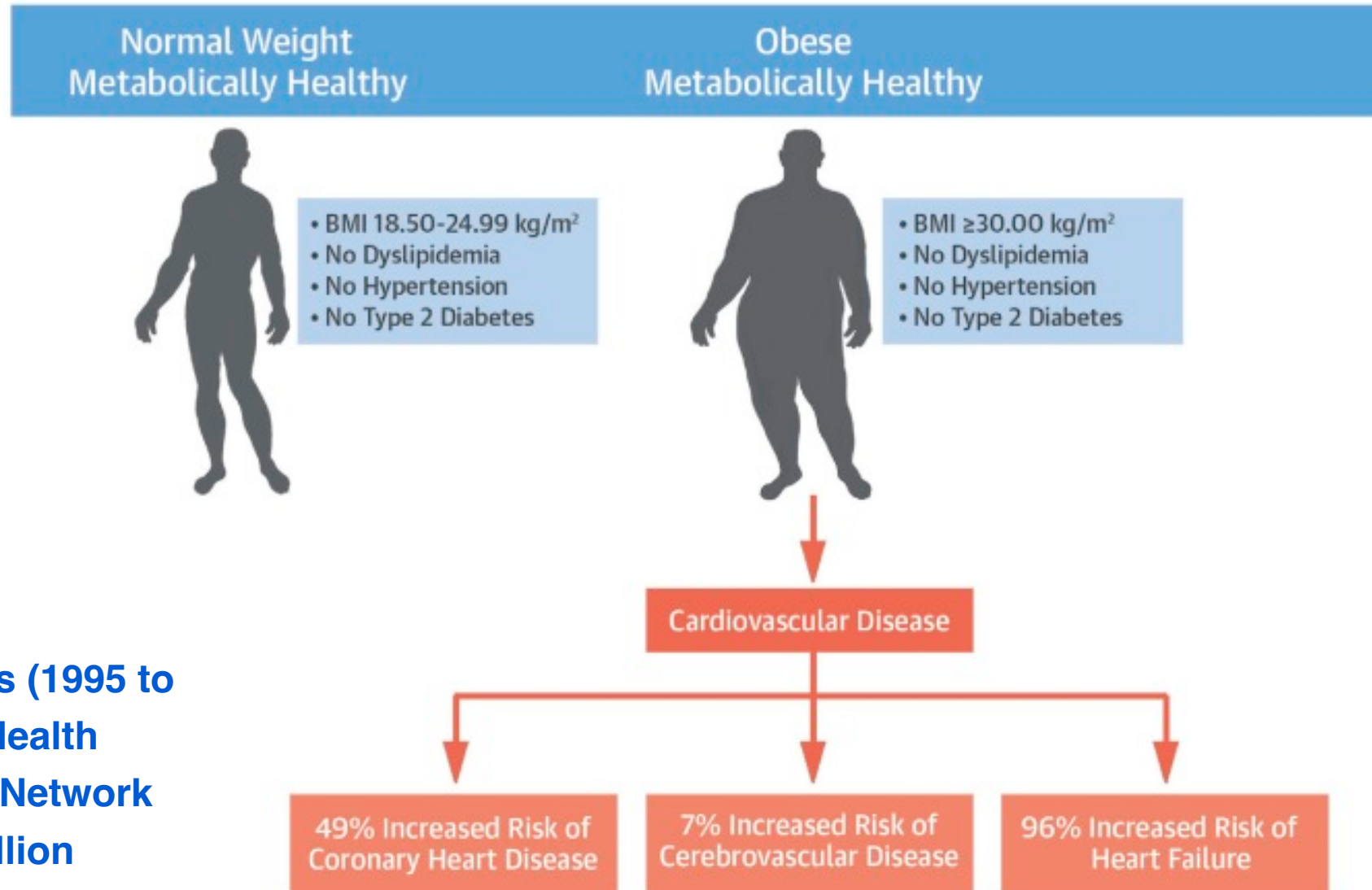
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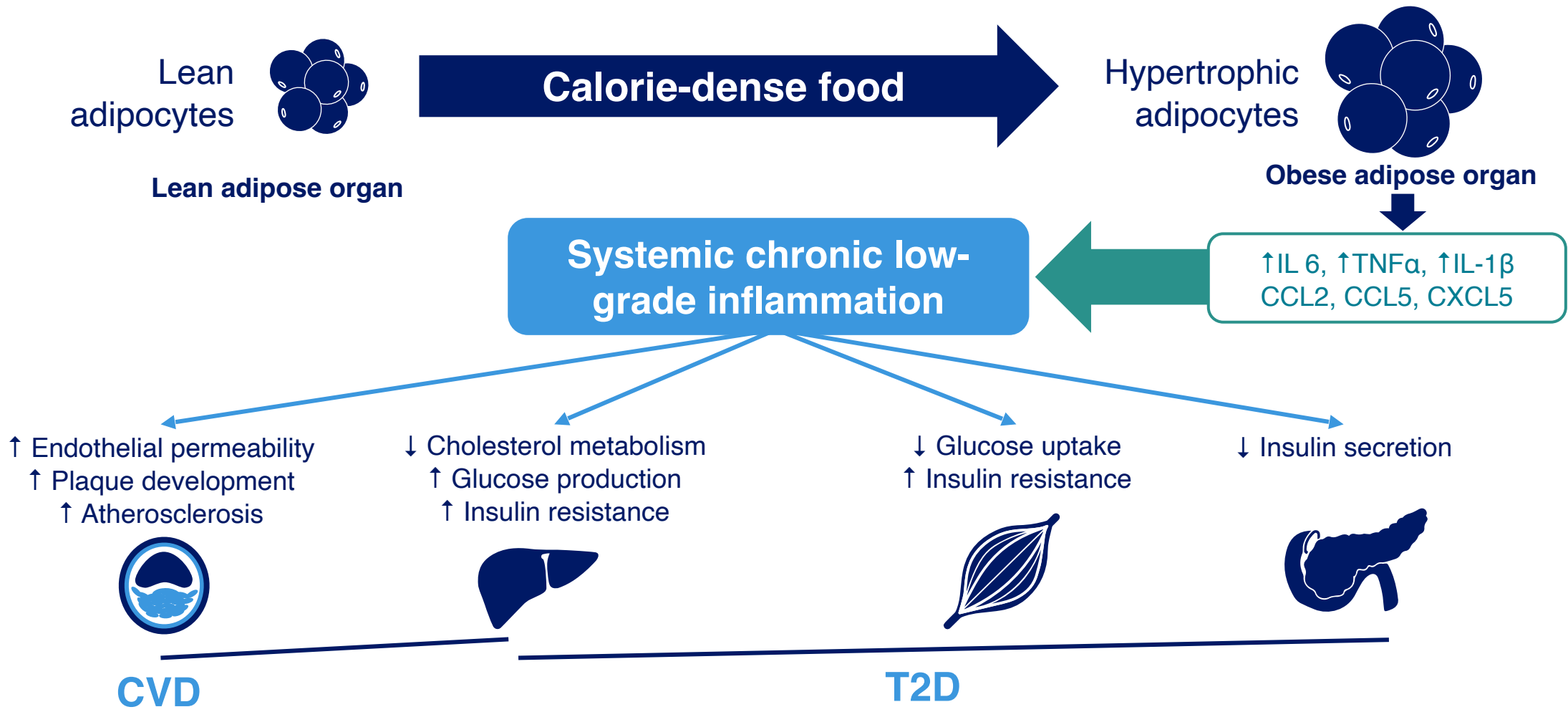
Metabolically Healthy Obese and Incident CVD



Health records (1995 to 2015) in The Health Improvement Network (THIN); 3.5 million individuals; 5.4 yrs FU

Systemic inflammation

Increases Risk of CVD and T2D



CCL, chemokine (C-C motif) ligand; CVD, cardiovascular disease; CXCL5, chemokine (C-X-C motif) ligand 5; IL, interleukin; T2D, type 2 diabetes; TNF α , tumour necrosis factor alpha.

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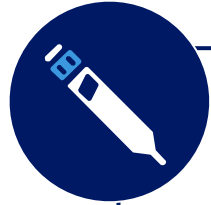
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Obesity
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Semaglutide mechanism of action

Appetite and weight regulation



Semaglutide is a human GLP-1 analogue

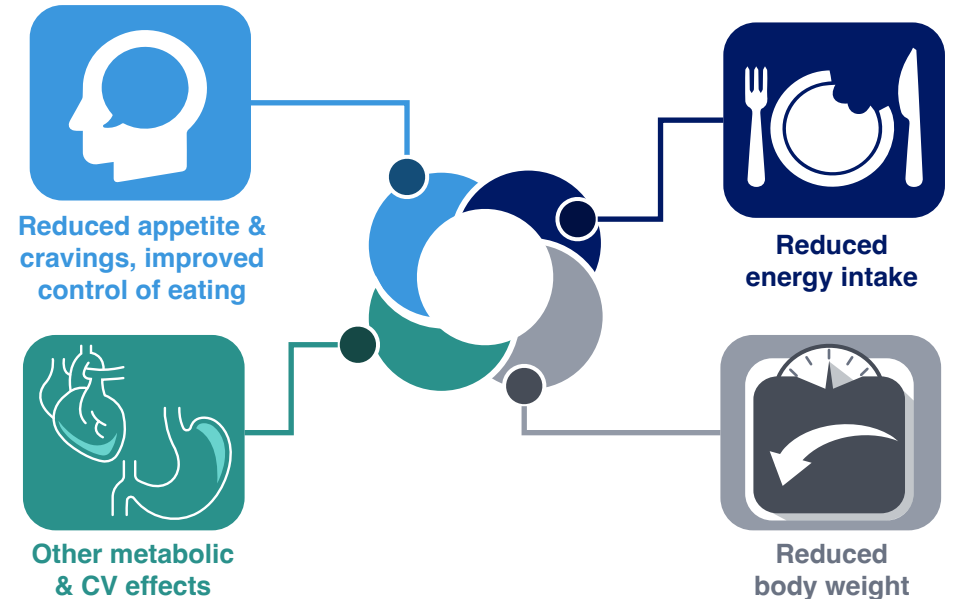
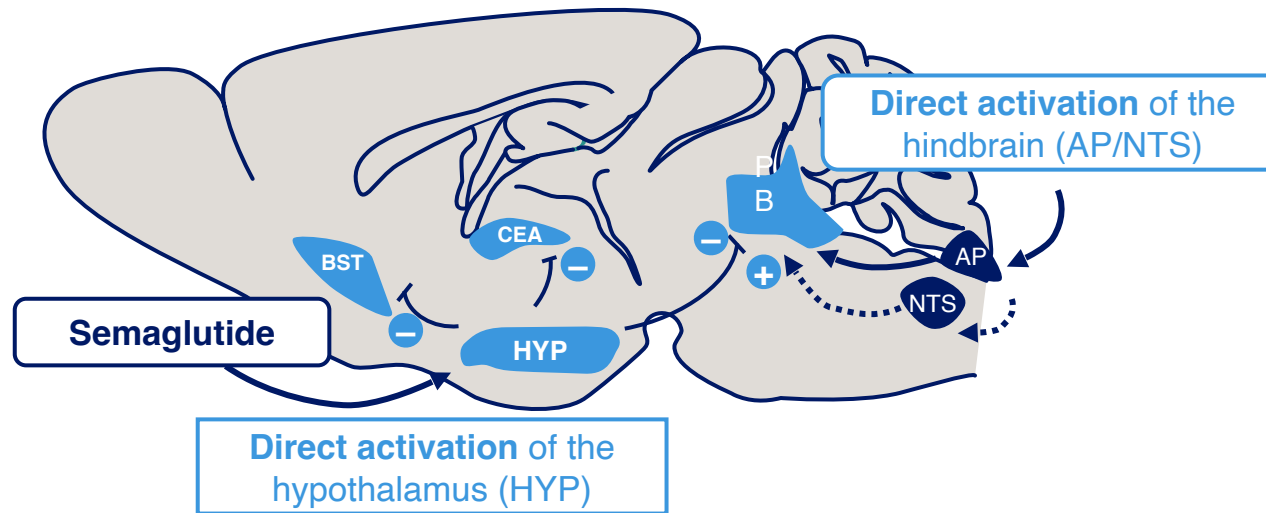
- 94% homology to human GLP-1
- $t_{1/2}$ of approximately 1 week

Amino acid substitution at position 8
(alanine to alpha-aminoisobutyric acid)
protects against DPP-4 degradation¹

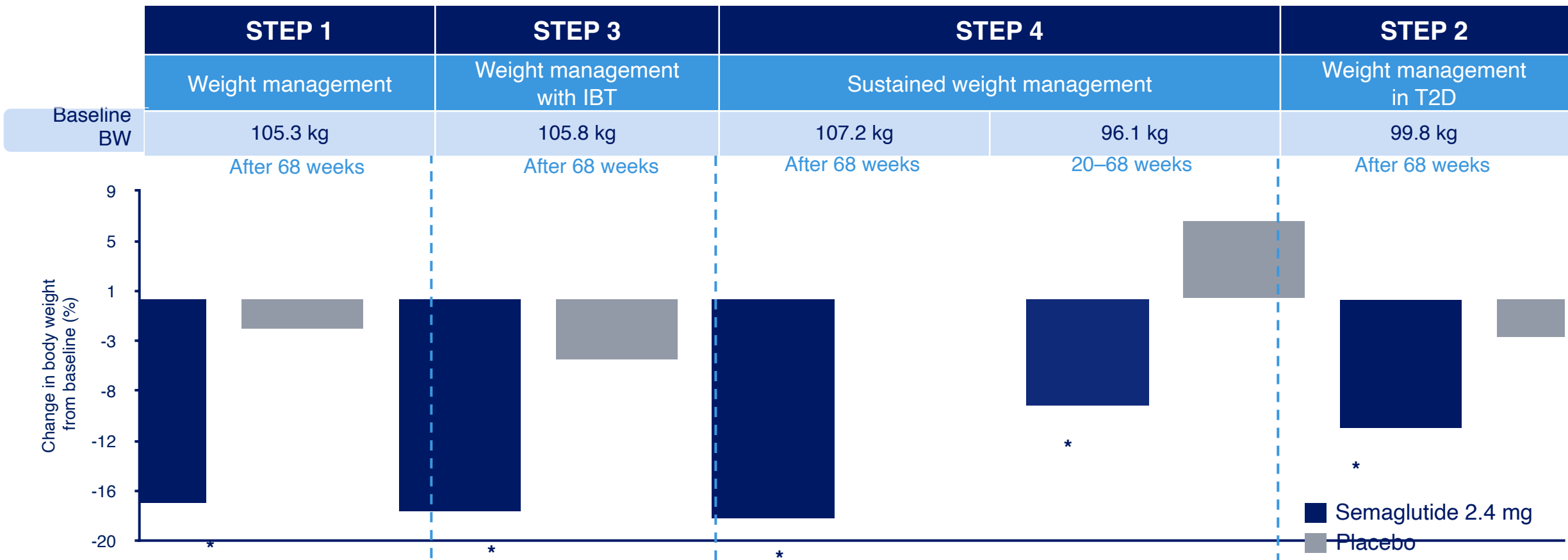
Spacer and C-18 fatty di-acid chain to
lysine in position 26 provide strong binding to
albumin



Amino acid substitution at position 34 (lysine to arginine) prevents
C-18 fatty di-acid binding at the wrong site



Weight Loss Across STEP Global Phase 3a Trials

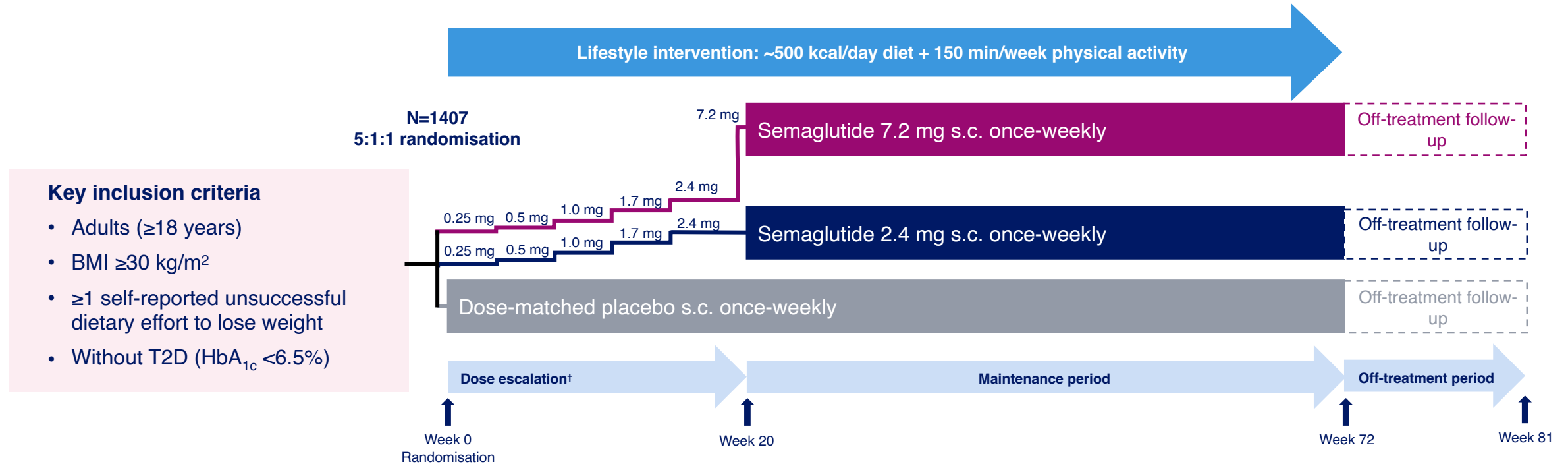


Trial product estimand: Evaluates the treatment effect under the assumption that the trial product is taken as intended

STEP UP

Trial Design

Randomised, double-blind, multinational, placebo- and active-controlled trial



Trial endpoints

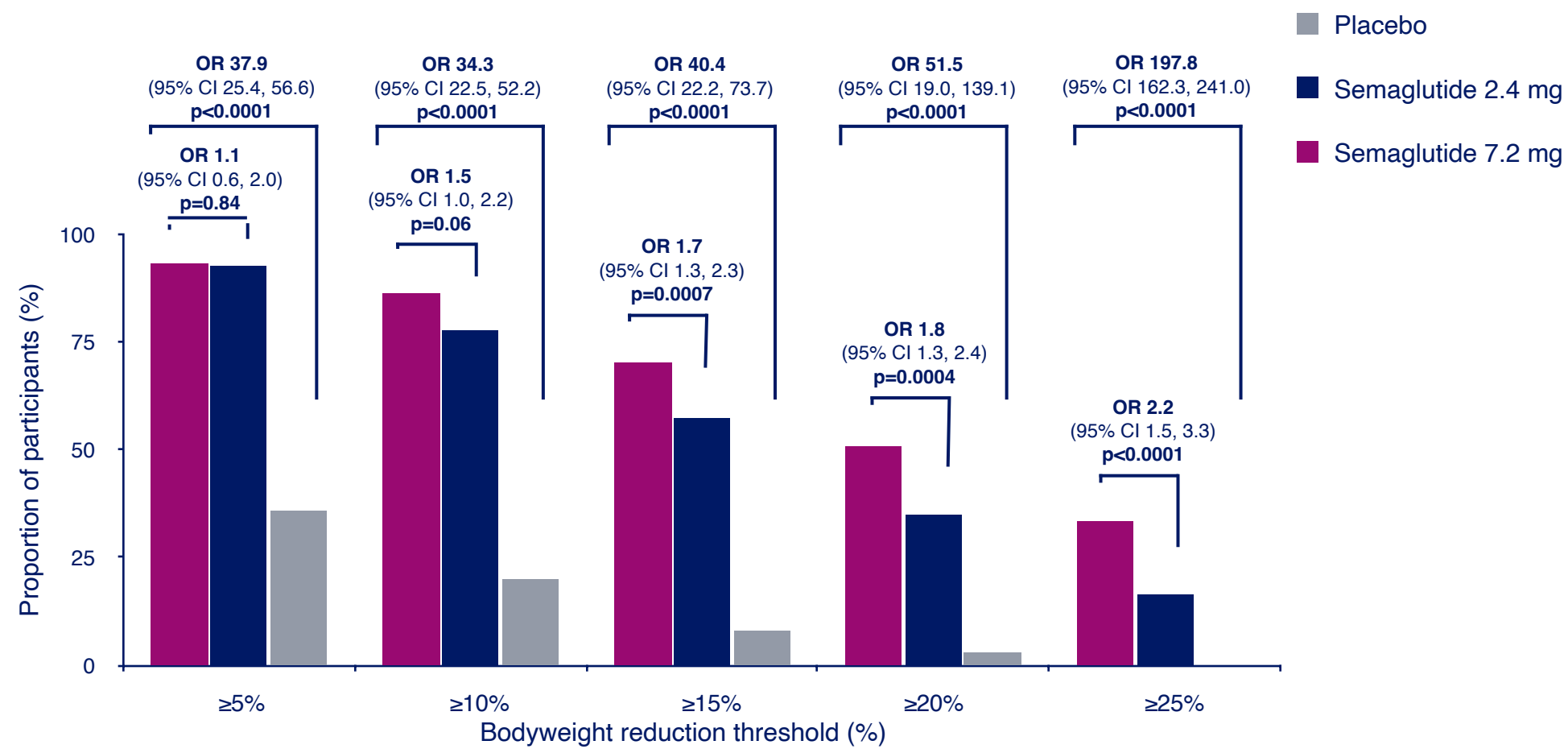
Coprimary *: at week 72, change in body weight (%) and proportion of participants achieving body weight loss of $\geq 5\%$

Secondary: at week 72, proportion of participants achieving body weight loss of $\geq 10\%$, $\geq 15\%$, $\geq 20\%$, and $\geq 25\%^*$, change in waist circumference (cm)*, change in body weight (%)†, proportion of participants achieving weight loss of $\geq 20\%$ and $\geq 25\%^†$

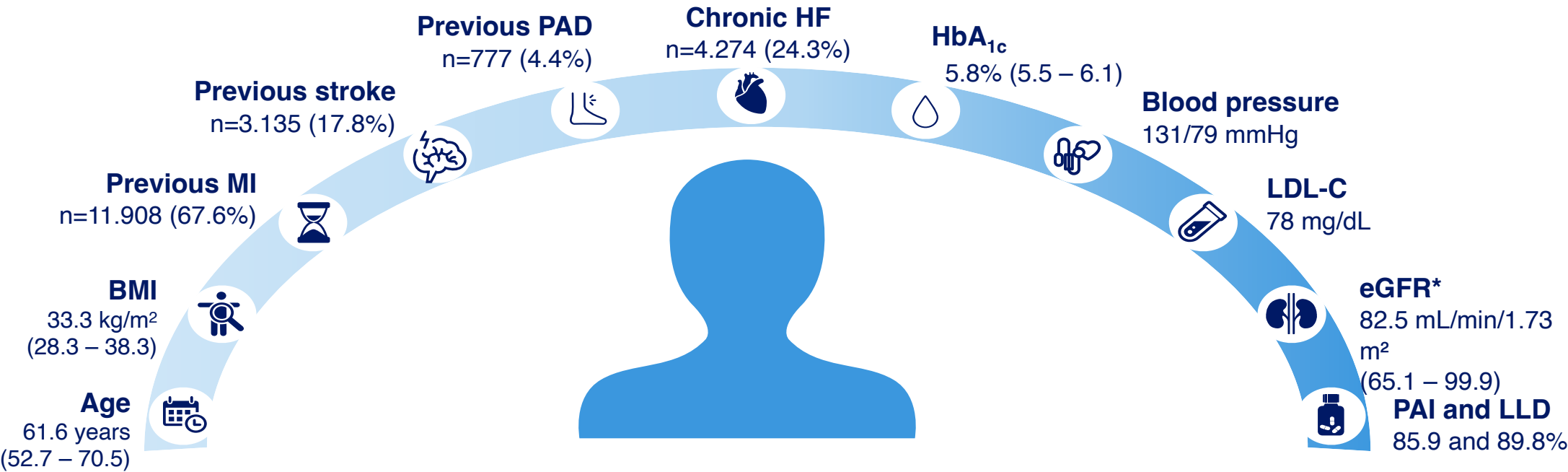
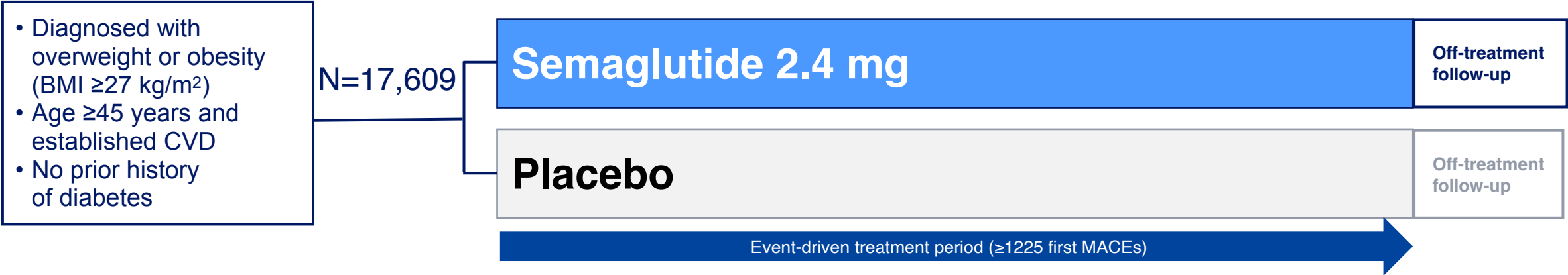
Safety: assessed by monitoring AEs‡

STEP UP

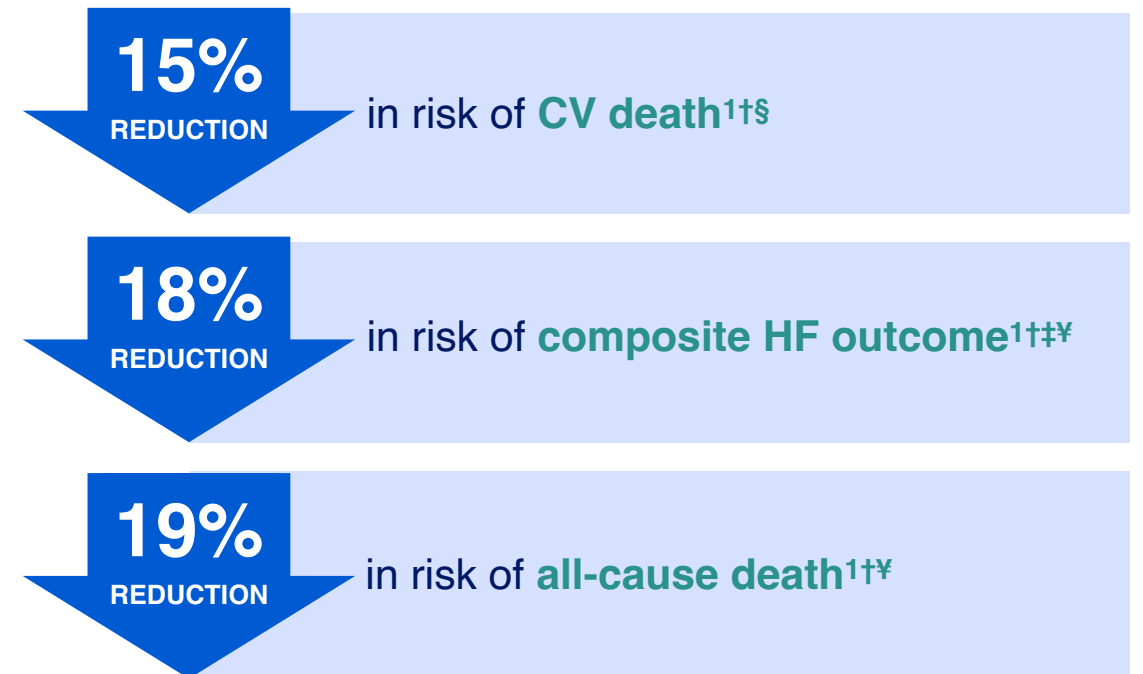
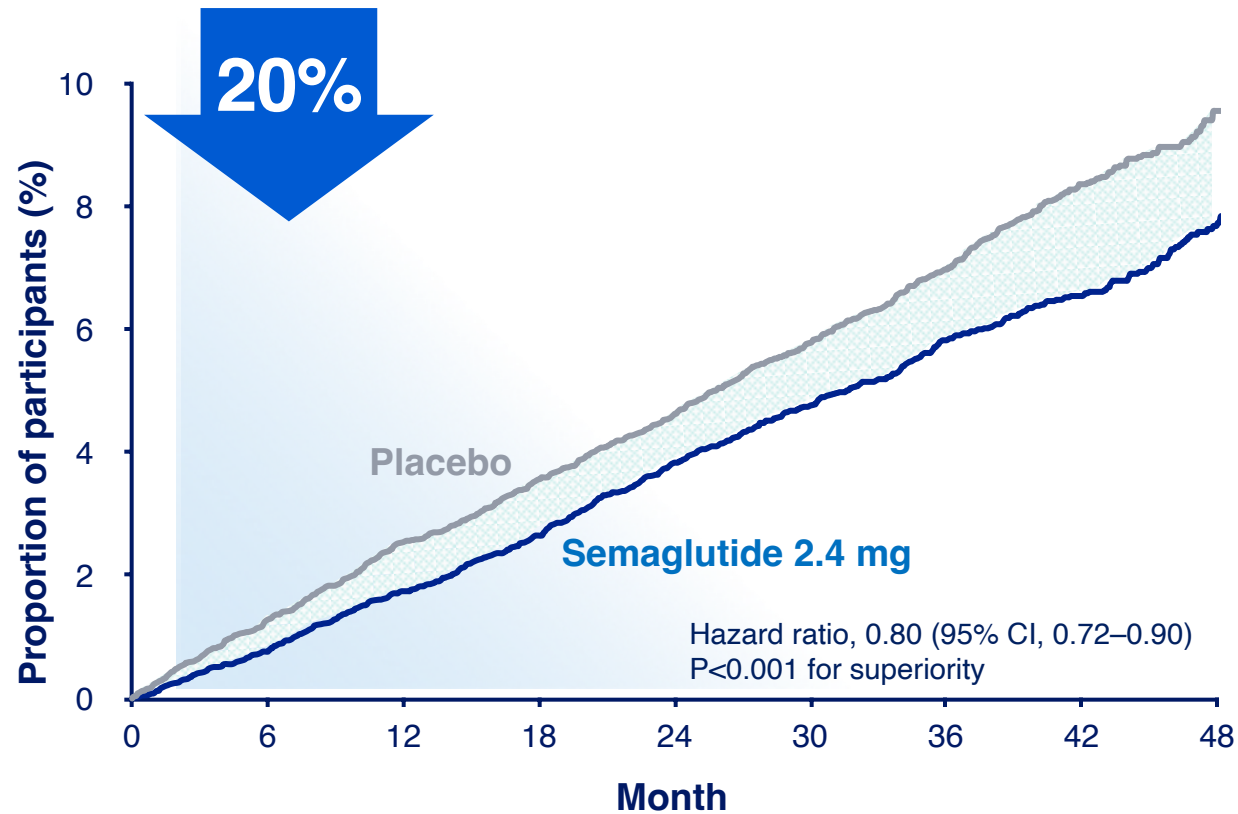
Categorical Body Weight Loss



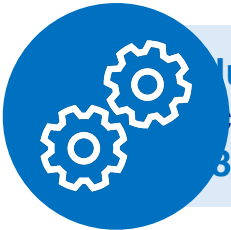
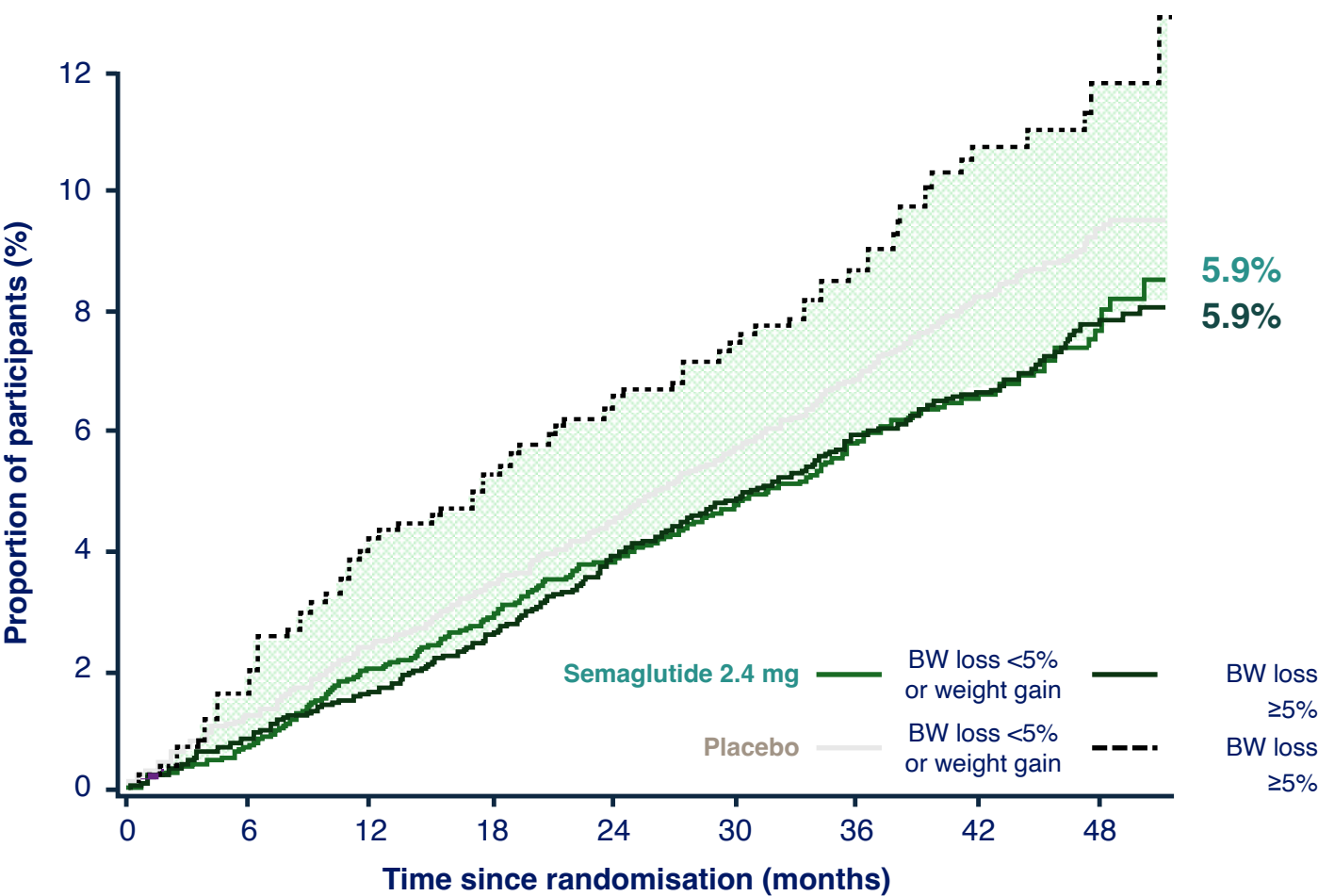
SELECT: Semaglutide CVOT



SELECT Results At a Glance



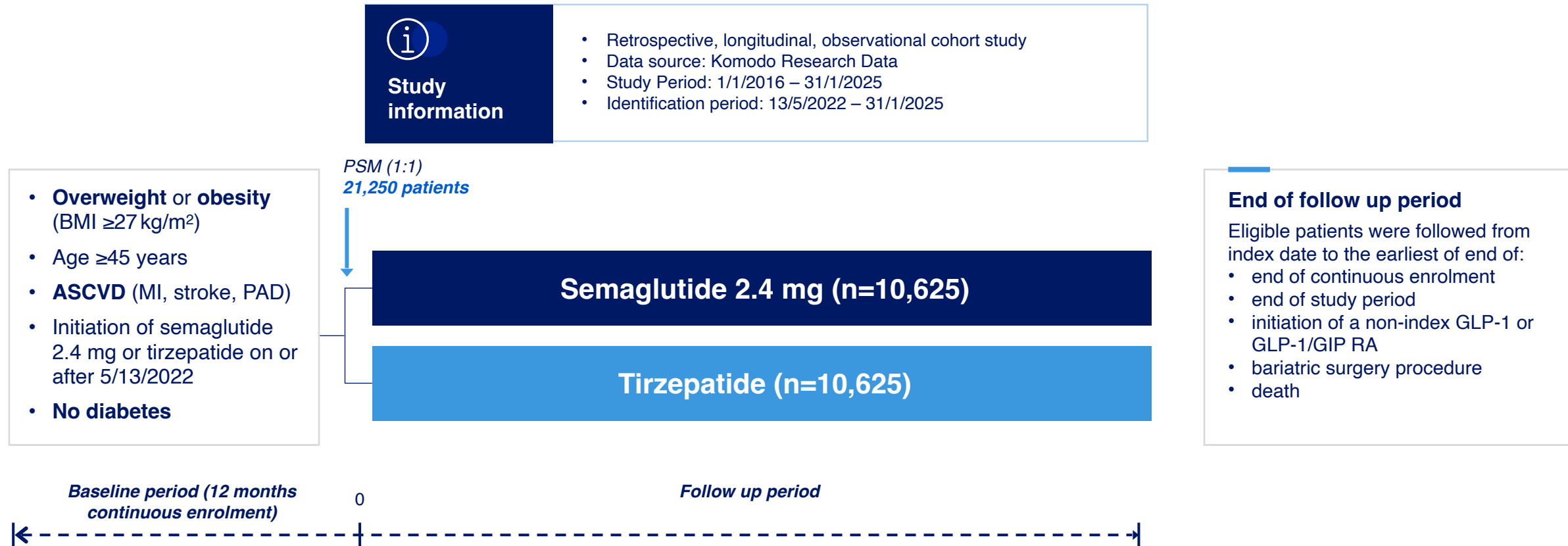
The MACE Risk Reduction with Semaglutide is Independent of Changes in Body Weight at Week 20



Value for interaction between MACE risk reduction and changes in body weight is 0.1334

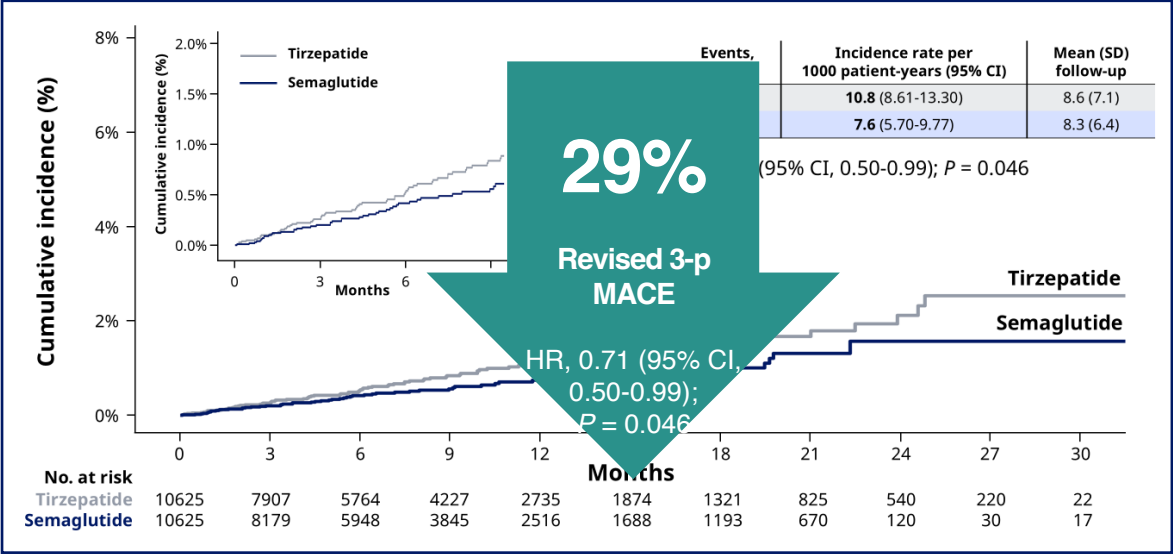
	HR (95% CI)	p-value
BW loss <5% or weight gain	0.85 (0.72, 1.00)	0.1334
BW loss ≥5%	0.67 (0.52, 0.87)	

STEER: Study Design



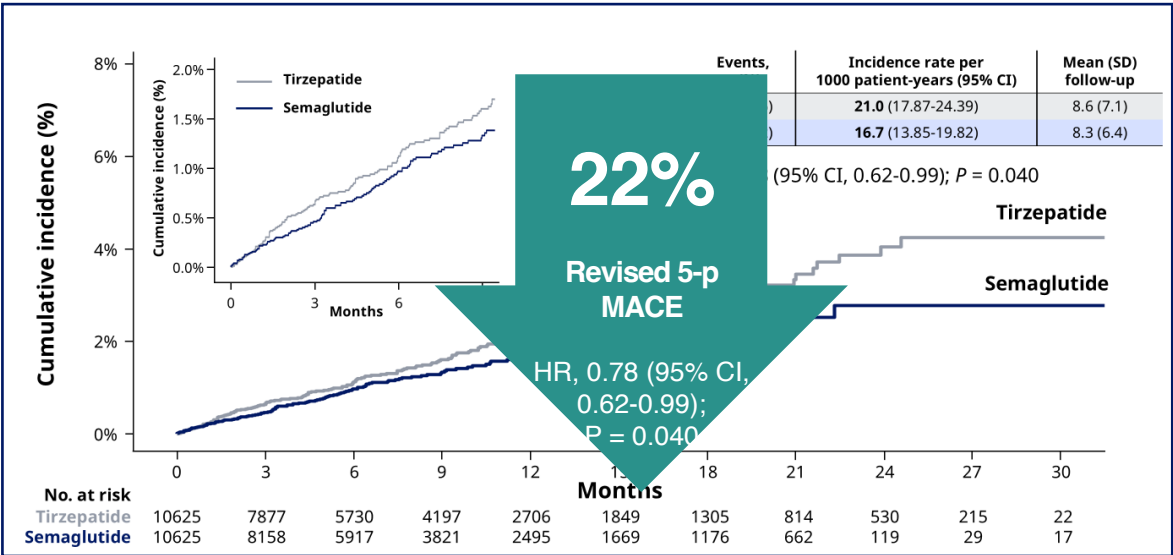
STEER: ITT Analysis

r3p-MACE



MI, stroke and all-cause mortality

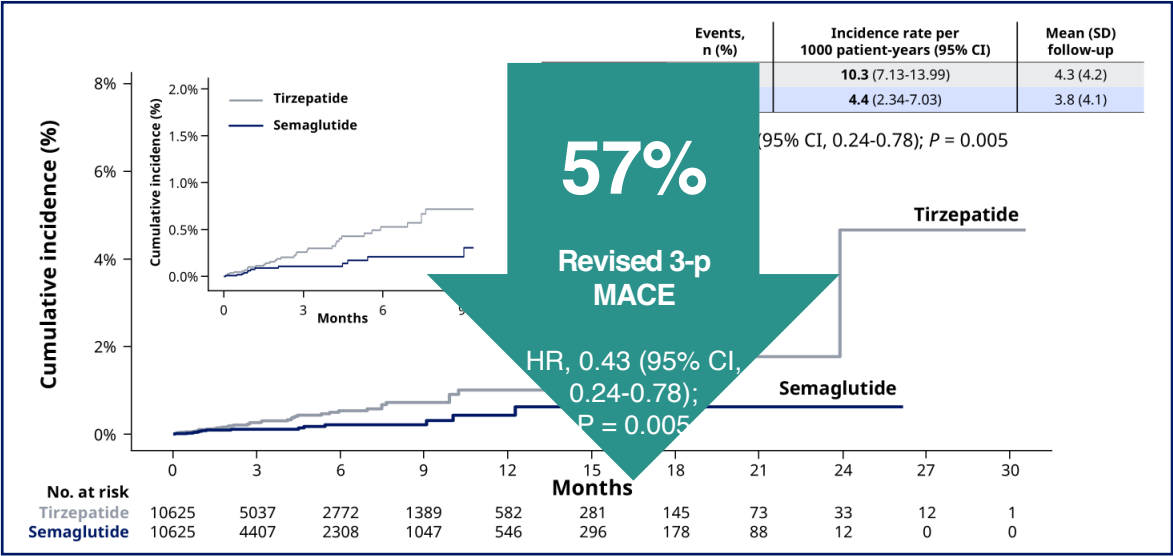
r5p-MACE



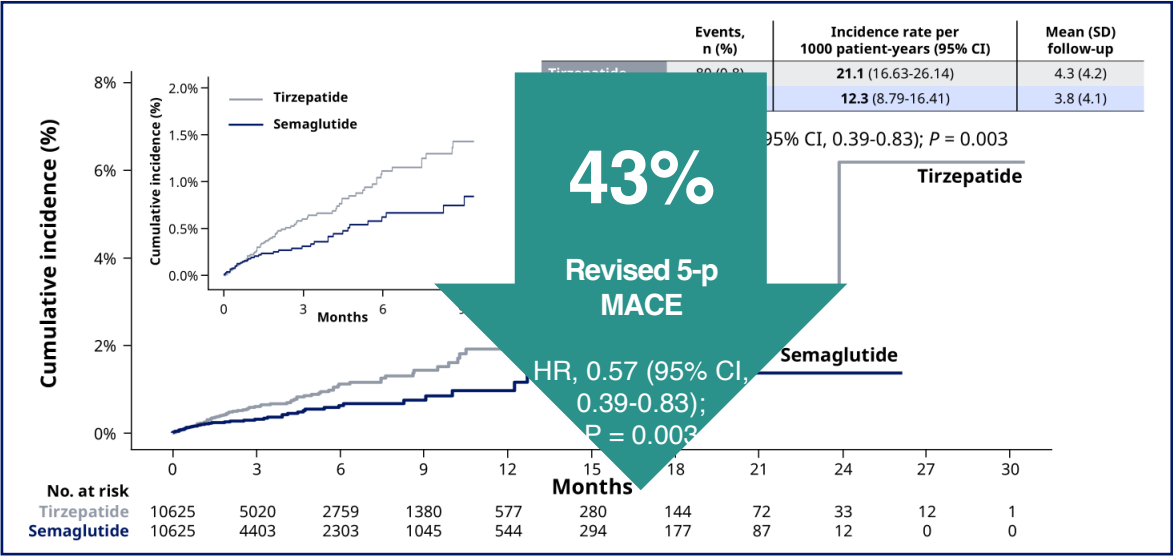
MI, stroke, hospitalization for HF, coronary revascularization procedure, and all-cause mortality

STEER: PP Analysis

r3p-MACE



r5p-MACE



Summary

More than half the world population is projected to have overweight or obesity by the year 2035;

High BMI is estimated to have accounted for 4 million deaths globally in 2015, more than 2/3 of which were caused by CVD;

Obesity should no longer be considered as a CV risk factor but a complex disease with important implications on CV outcomes that should be treated appropriately;

Semaglutide provides CV benefits in obese/overweight pts that extend beyond weight loss, uniquely improving outcomes through direct metabolic, anti-inflammatory and vascular effects